

- 27 -

## WHAT IS CLAIMED:

- Sub B' 5
1. A nonhuman transgenic animal comprising a modified GP V gene.
  2. The animal of claim 1 wherein the animal is a mammal selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.
  - Sub B2 10 3. Platelets isolated from the blood plasma of the animal of any of claims 1 or 2.
  4. The mammal of claim 2 which is a mouse.
  - Sub B3 15 5. A method of preparing a nonhuman, transgenic mammal with a modified GP V gene, said method comprising:
    - a) introducing into embryonic stem cells a nucleic acid molecule encoding a modified GP V gene; and
    - b) regenerating a transgenic nonhuman mammal from the cells resulting from step a).
  - 20 6. The method of claim 5, wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.
  7. The method of claim 6 wherein the non-human mammal is a mouse.
- 25

- 28 -

8. The method of claim 5 further comprising the step of breeding the transgenic nonhuman mammal so as to produce a nonhuman mammal homozygotic for the modified GP V gene.

5

9. The method of claim 8 wherein the non-human mammal is a mouse.

10. A method of preparing a nonhuman, transgenic mammal with a nonfunctional GP V gene, said method comprising:

10

- a) introducing into embryonic stem cells a nucleic acid molecule encoding a disrupted or nonfunctional GP V gene and a selectable marker ;
- b) identifying and selecting transformed cells;
- c) injecting the transformed cells from step c) into blastocysts; and,
- d) regenerating a nonhuman transgenic mammal from the blastocysts of step c), wherein the regenerated nonhuman transgenic mammal is chimeric for the nonfunctional GP V gene.

15

11. The method of claim 10 wherein the nonhuman mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

20

12. The method of claim 11 wherein the nonhuman mammal is a mouse.

13. The method of claim 10 further comprising the following steps:

Sub 79  
C le

- 29 -

- 5
- Sub C6)
- e) breeding the chimeric nonhuman mammal with a wild-type nonhuman mammal to produce a nonhuman mammal heterozygotic for the nonfunctional GP V gene;
  - f) crossing a heterozygotic nonhuman mammal produced in step e) with a chimeric non-human mammal or a heterozygotic nonhuman mammal; and,
  - g) selecting a nonhuman mammal homozygotic for the nonfunctional GP V gene from the resulting progeny.

14. The method of claim 13 wherein the non-human mammal is a mouse.

10

Sub B)

15. A method to identify an agent that modulates a biological response of a nonhuman transgenic mammal having a modified GP V gene, comprising the step of exposing the mammal to the agent and determining whether the agent modulates the response.

15

16. The method of claim 15 wherein the transgenic mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

17. The method of claim 16 wherein the transgenic mammal is a mouse.

20

18. The method of claim 15 wherein the response is a thrombotic response.

19. The method of claim 15 wherein the response is an angiogenic response.

25

20. The method of claim 15 wherein the response is an inflammatory response.

- 30 -

21. A method of determining the effect of an agent on a characteristic of an animal that is attributable to the expression of the GP V gene, said method comprising;

- a) administering said agent to the animal of claim 1;  
b) maintaining said animal for a desired period of time after said administration;  
and,  
c) determining whether a characteristic of said animal that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.

22. The method of claim 21 wherein the animal is a mouse.

23. An cell line isolated from a nonhuman transgenic mammal that contains a transgene stably integrated into the mammal's genome, said transgene encoding a modified GP V gene.

24. The cell line of claim 23, wherein said transgene has been introduced into said nonhuman mammal or an ancestor of said nonhuman mammal via homologous recombination in embryonic stem cells, and further wherein said nonhuman mammal expresses a modified GP V protein.

25. The cell line of claim 23 wherein said nonhuman mammal is a mouse.

26. The cell line of claim 25, wherein said mouse is fertile and transmits the nonfunctional GP V gene to its offspring.

27. The cell line of claim 23, wherein the modified GP V protein is nonfunctional.